



10037591 . 082202

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Figure 1

Map of Human IL-17 Like cDNA (SEQ ID NO:1) and
Amino Acid (SEQ ID NO:2) Sequences

1	CTCAAGTCACTCCCTAAAAGACAGTGGAAATAAATTGAATAAACAACAGGCTTGCT	8
61	GAAAATAAATCAGGACTCCTAACCTGCTCCAGTCAGCCTGCTTCCACGAGCCTGTGTCAG	28
121	TCAGTGCCCCACTTGTGACTGAGTGTGCAGTGCCCCAGCATGTACCAGGTGGTTGCATTCT	48
1	<u>M Y Q V V A F L</u>	68
181	TGGCAATGGTCAATGGGAACCCACACCTACAGCCACTGGCCCCAGCTGCTGCCCCAGCAAAG	88
9	A M V M G T H T Y S H W P S C C P S K G	108
241	GGCAGGACACCTCTGAGGAGCTGCTGAGGTGGAGCACTGTGCTGCTGCTGCCCTCCCTAGAGC	128
29	Q D T S E E L L R W S T V P V P L E P	148
301	CTGCTAGGCCCAACCGCCACCCAGAGTCCTGTAGGGCCAGTGAAGATGGACCCCTCAACA	
49	A R P N R H P E S C R A S E D G P L N S	
361	GCAGGGCCATCTCCCCCTGGAGATATGAGTTGGACAGAGACTTGAACCGGCTCCCCCAGG	
69	R A I S P W R Y E L D R D L N R L P Q D	
421	ACCTGTACCACGCCCGTTGCCCTGTGCCCGCACTGCGTCAGCCTACAGACAGGCTCCCACA	
89	L Y H A R C L C P H C V S L Q T G S H M	
481	TGGACCCCCGGGCAACTCGGAGCTGCTTACCACCAACCAGACTGTCTTCTACCGCGGC	
109	D P R G N S E L L Y H N Q T V F Y R R P	
541	CATGCCATGGCGAGAAGGGCACCCACAAAGGGTACTGCTGAGCGCAGGCTGTACCGTG	
129	C H G E K G T H K G Y C L E R R L Y R V	
601	TTTCCTTAGCTTGTGTGTGTCGGGCCCGTGTGATGGGCTAG 643	
149	S L A C V C V R P R V M G * 162	

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Figure 2A

(Map of Mouse IL-17 Like cDNA (SEQ ID NO:3) and Amino Acid
(SEQ ID NO:4) Sequences with Predicted Signal Peptide

1 ATGTACCAGGCTGTTCATTTCTTGGCAATGATCGTGGGAACCCACACCGTCAGCTTG
M Y Q A V A F L A M I V G T H T V S L
58 CGGATCCAGGAGGCTGCAGTCACCTTGCCACAGCTGCTGCCCCAGCAAGAGCAAGAACCC
11 R I Q E G C S H L P S C C P S K E Q E P
118 CCGAGGAGTGGCTGAAGTGGAGCTCTGCATCTGTGTCCCCCAGAGCCTCTGAGCCAC
31 P E E W L K W S S A S V S P P E P L S H
178 ACCACACGAGAAATCCTGCAGGCGCAGCAAGGATGGCCCCCTCAACAGCAGGCGCATC
51 T H H A E S C R A S K D G P L N S R A I
238 TCTCCTTGGAGCTATGAGTTGGACAGGGACTTGAATCGGGTCCCCCAGGACCTGTACCAC
71 S P W S Y E L D R D L N R V P Q D L Y H
298 GCTCGATGCCCTGTGCCACACTGCGTCAGCCTACAGACAGGCTCCACATGGACCCGCTG
91 A R C L C P H C V S L Q T G S H M D P L
358 GGCAACTCCGTCCTTACCACAACCAAGACGGTCTTCTACCGGGCCATGCCATGGC
111 G N S V P L Y H N Q T V F Y R R P C H G
418 GAGGAAGGTACCCATCGCCGCTACTGCTTGGAGCGCAGGCTCTACCGAGTCTCCTTGGCT
131 E E G T H R R Y C L E R R L Y R V S L A
478 TGTGTGTGTGCGGCCCCGGTTCATGGCTTAGTCATGCTCACCACCTGCCTGAGGCTGA
160 C V C V R P R V M A *
538 TGCCCGGTTGGAGAGAGGGCCAGGTGTACAAATCACCTTGCCCAATGCGGGCGGTTCAA
598 GCCCTCCAAGCCCTACCTGAAGCAGCAGGCTCCCGGACAAAGATGGAGGACTTGGGGAG
658 AAACCTGACTTTTGCACACTTTTGGGAAGCACTTTTGGGAAGGAGCAGGTTCCCGCTTGTGC

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Figure 2B

718 TGCTAGAGGATGCTGTTGTGGCAATTTCTACTCAGGAACGGACTCCAAAGGCTGTGACC
778 CTGGAAGCCATACTCCTGGCTCCTTTCCCTGAATCCCCAACTCCTGGCACAGGCACTT
838 TCTCCACCTCTCCCCCTTTGGCTTTTGTGTTTGTGTCATGCCAACTCTGCGTGC
898 AGCCAGGTGTAATTGCCCTTGAAGGATGGTTCTGAGGTGAAAGCTGTTATCGAAAGTGAAG
958 AGATTATCCAAATAAACATCTGTGTTTAAAAAATAAAAAAATAAAAAA 1496

Map of Non-Secreted Form of Mouse IL-17 Like cDNA (SEQ ID NO:9), and
Corresponding Amino Acid Sequence (SEQ ID NO:10)

1 CCGGCAGGTGCCCTCGGCGCGTCCCAAAGCTTAGGGAAGCTCCAGGTGCTTGGAAT
61 GAAGAAAAGGCCACCGAGCAAAAAGGAACAGAGAGGGGAGGAGCAGTGCTGTGGGCTC
121 GCCTAGGTCGAGGGCCATTATCACCTACAAATCAGAAATGTGGAGTGCTATCTAGAGG
181 TCTCCATCTTTGCCATTGCTGGTGCCTCAGAAAAGTGATGGGTTGTCCCATTTGCCA
241 AGAACAGCTTCTGCTTACCAGCAGGTGCTGACCTCTTTCCCAAGGCACAGGGAAGGAA
301 TTCCAGCCCCGGTTGGCTGCCAGAGGCTTCTCTGGCTTGGGTACAGAGGCAGAGAAAG
361 AAACCCCAAATGTCTCCATGAAAACAAATGTCCCGTCAATCCAGGCCAGATCATCTGC
421 AGTGTCAACAGTTGAGACAAGAGCTGGGTCTATTTCTGTGCCCTAAGAGTGCCGTCTT
481 GCAC TGGCC AAGGCTGTGCAATCTTGGCAATGATCGTGGGAACCCACACCGTCAGCTTG
M I V G T H T V S L
541 CGGATCCAGAGGGCTGCAGTCACTTGCCCCAGCTGTGCCCCAGCAAGAGCAAGAACCC
11 R I Q E G C S H L P S C C P S K E Q E P 30

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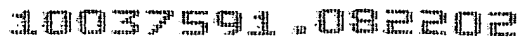


Figure 2C

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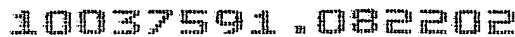


Figure 3A

(SEQ ID NO:5)

Smith-Waterman score: 155; 25.0% identity in 160 AA overlap

hIL-17L	10	20	30	40	50	60
	XNQDSXPAPVSL	PRGLSVSAPLV	TECAVPSMYQV	VAFLAMVMG	THTYSHWPS	CCPSKQ
			: :::	:	: :	: :
hIL-17			MTPGKTS	LVSLLLL	SLLEAIVK	AGITIPRNP
			10	20	30	
						SEDK
hIL-17L	70	80	90	100	110	120
	DTSEELRWSTV	VPPLPARPNR	HPESCRA	SEDGPLNS	RAISPWR	YELDRDLN
	:	:	:	:	:	:
	:	:	:	:	:	:
hIL-17	NFPRTVMVNL	NI-----	HNRNTNTN	PK--RSSD	---Y	YNRSTSPW
	40	50	60	70	80	
						NLHRNEDPER
						YPSVI

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Figure 3B

	130	140	150	160	170	180
hIL-17L	YHARCLCPHCVSLQ	TGSHMDPLGNSV	PLYHNQTVFYRR	PCHEEGTHRRY	CYCLERRLYRVS	
	:: :	:: :	:: :	:: :	:: :	
hIL-17	WEAKCRHLGCIN--	ADGNVDYHMNSV	PIQQEILVLRRE	PPHCPNS----	FRLEKIL--VS	
	90	100	110	120	130	140

	190
hIL-17L	LACVCVRPRVMA
	:: :
hIL-17	VGCTCVTPIVHHVA
	150

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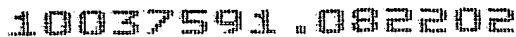


Figure 4

SCORES Init1: 124 Initn: 124 Opt: 175
Smith-Waterman score: 175; 36.7% identity in 90 aa overlap

	130	140	150	160	170	180
hIL-17L	PHCVSLQTGSHMDPLGNSVPLYHNQTVFYRRPCHGEEGTHRRYCLERRLYRVSLA-CVCV					
	: :	: :	: :			: : : : : :
hIL-20	LGCVPNPFMTQE-DRSMVSVPVF-SQVPVRRRLCPPPPRTGP--CRQRAVMETIVAGCTCI					
	130	140	150	160	170	180

hIL-17L
190 RPRVMA

hIL-20 F

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Figure 5

Pile-Up of Human IL-17 Like Amino Acid Sequence, hIL-17L, (SEQ ID NO:2)
with a Known Human IL-17 Amino Acid Sequence, hIL-17b (SEQ ID NO:7)

Family Member

SCORES Init1: 124 Initn: 124 Opt: 178
Smith-Waterman score: 178; 35.6% identity in 90 aa overlap

hIL-17L	70	80	90	100	110	120
	RWSTVPVP	PLEPARPNRHPESCRASEDGPLNSRAISPWRYELDRDLNRLPQDLYHARCLC				
hIL-17b	70	80	90	100	110	120
	RNIEEMVAQLRNSSELAQRKCEVNQLWMSNKRSLSPWGYGINHDPSPRIPVDLPEARCLC					
hIL-17L	130	140	150	160	170	180
	PHCVSLQ	TGSHMDPLGNSVPLYHNQTVFYRRPCHGEEGTHRRYCLERRLYR-VSLACVCV				
hIL-17b	130	140	150	160	170	
	LGCVNPFTMQE-DRSMVSVPVF-SQVPVRRRLCPPPPRTGP--CRQRAVMETI					

hIL-17L
RPRVMA

hIL-17b
F

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Figure 6A

Pile-Up of Human IL-17 Like Amino Acid Sequence, hIL-17L, (SEQ ID NO:2)
with Amino Acid Sequence of a Known Human IL-17 Family Member,
hIL-17c (SEQ ID NO:8)

SCORES Init1: 149 Initn: 194 Opt: 236

Smith-Waterman score: 243; 34.5% identity in 171 aa overlap

hIL-17L	20	30	40	50	60	69
	GLSVSAPLVTECAVPSMYQVVAFLAMVMGTHTYSHW-PSCCPSK----					GQDTSELLR--
	: :	:	:	:	:	:
hIL-17c	10	20	30	40	50	
	MTLLPGLLFLTWLHTCLAHHDPSLRGHPHSHGTPHCYSAEELPLGQAPPHLLARGA					
hIL-17L	70	80	90	100	110	
	-WS-TVVPV-----PLEPARP-NRH--PES---C---RASE--DGPLNSRAISPWRYELDRD					
	: :	:	:	:	:	:
hIL-17c	60	70	80	90	100	110
	KWGQALPVALVSSLEAASHRGRHERPSATTQCPVLRPFEVLEADTHQRSISPWRYRVDTD					

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Figure 6B

hIL-17L	120	130	140	150	160	169
	LNRLPQDLYHARCLCPHCVSLQ	TGSHMDPLGNSVPLYHNQ	TVFYRRPCHGEEG	----	THR	
	:	:	:	:	:	:
	:	:	:	:	:	:
	:	:	:	:	:	:
hIL-17c	120	130	140	150	160	170
	EDRYPQKLAFACLCRCIDARTG	RETAAL-NSVRLLQSL	LVLR	RRPC-SRDG	SGLPTPG	
	:	:	:	:	:	:
	:	:	:	:	:	:
	:	:	:	:	:	:
hIL-17L	170	180	190			
	RYCLERRLYRVSLACV	VRPRVMA				
	:	:	:	:	:	:
	:	:	:	:	:	:
hIL-17c	180	190				
	AFAFHTEFIHVPVGCTC	VLPRSV				

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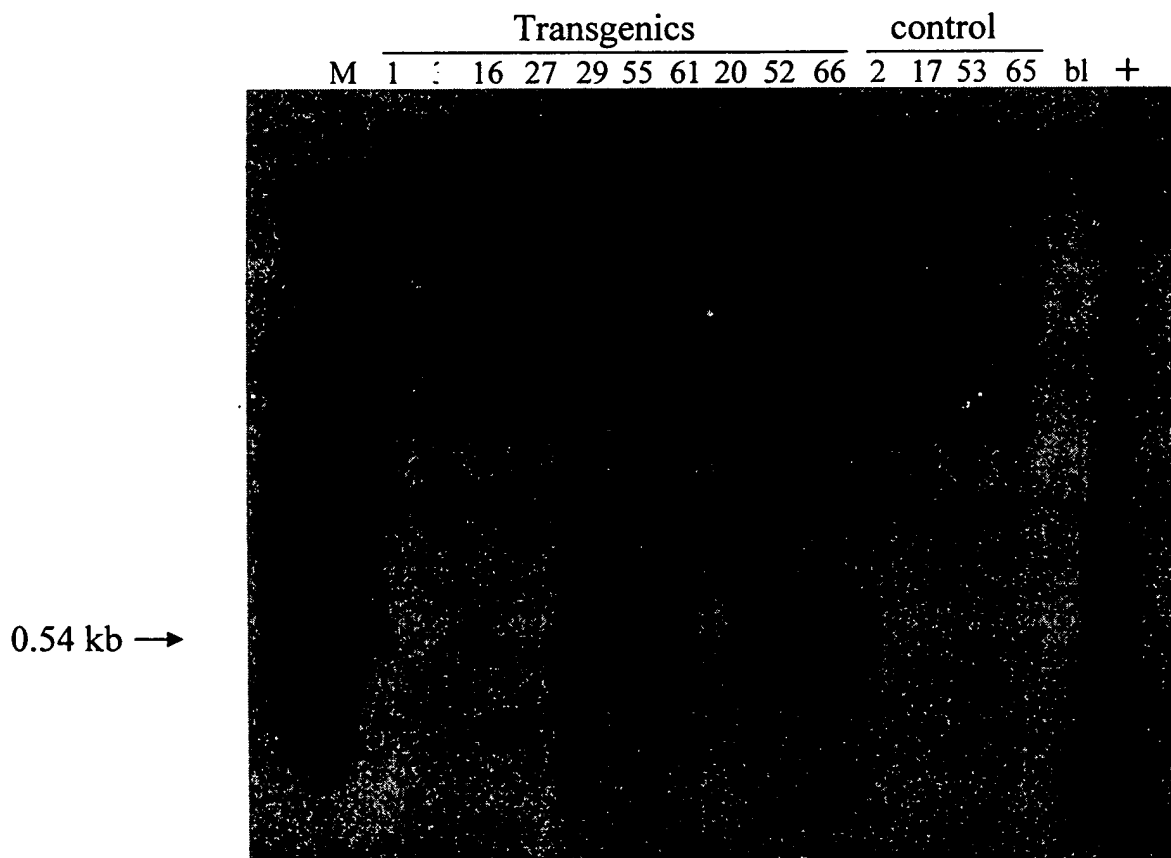
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Figure 7

Northern Blot Expression Analysis of TH00-018 Necropsied Transgenic Founders



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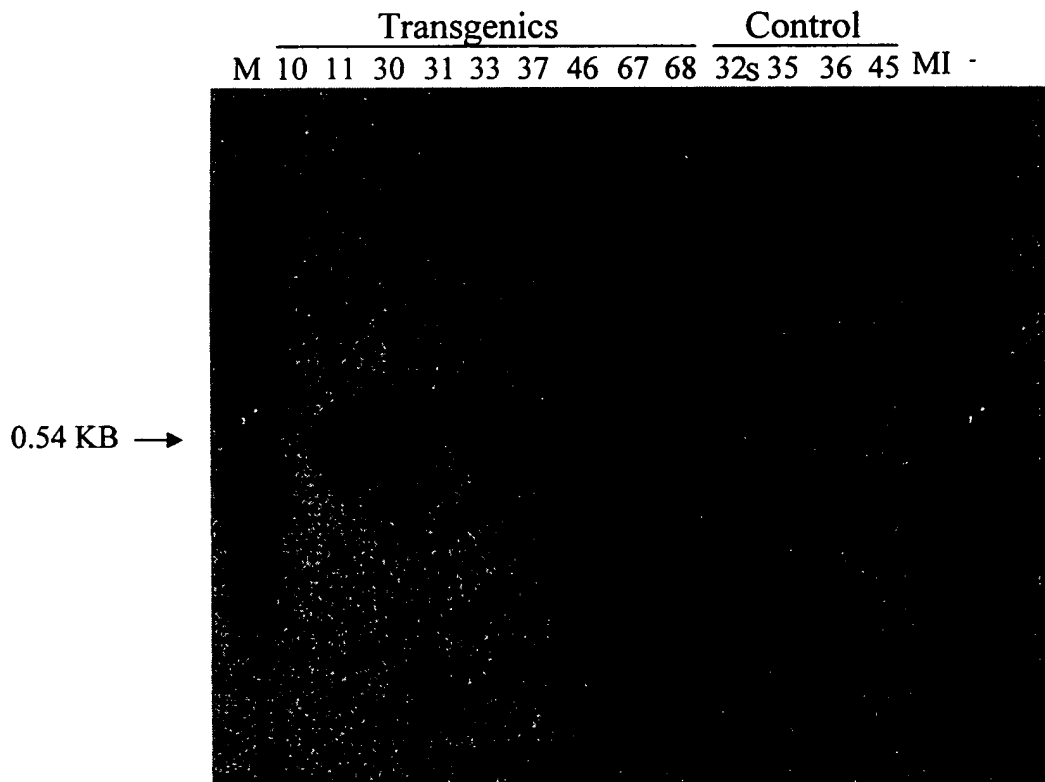
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Figure 8

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Northern Blot Expression Analysis of TH00-018
Hepatectomized Transgenic Founders



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Figure 9

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Non-Transgenics

IL-17E Transgenics

A



Lymph Node

B



C



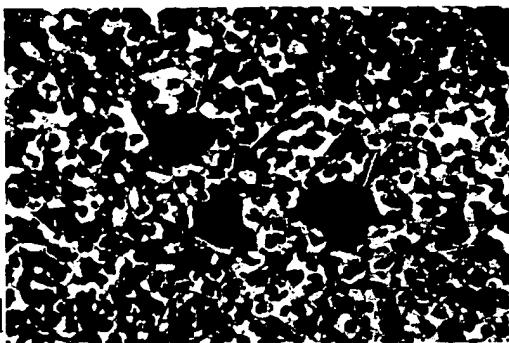
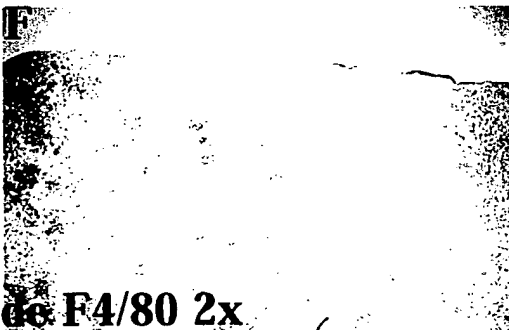
Lymph Node B220 2x



E



Lymph Node F4/80 2x



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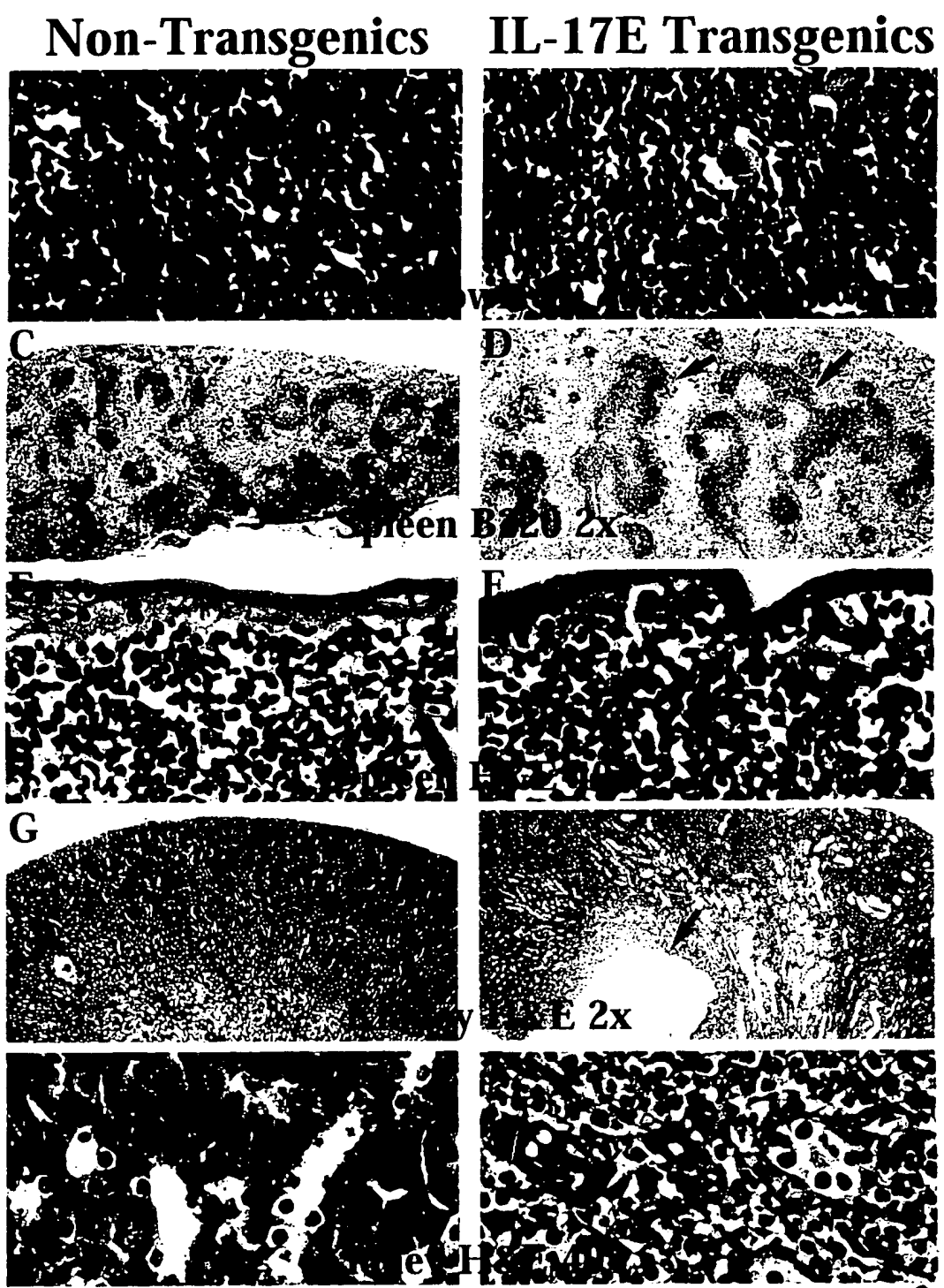
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Figure 10



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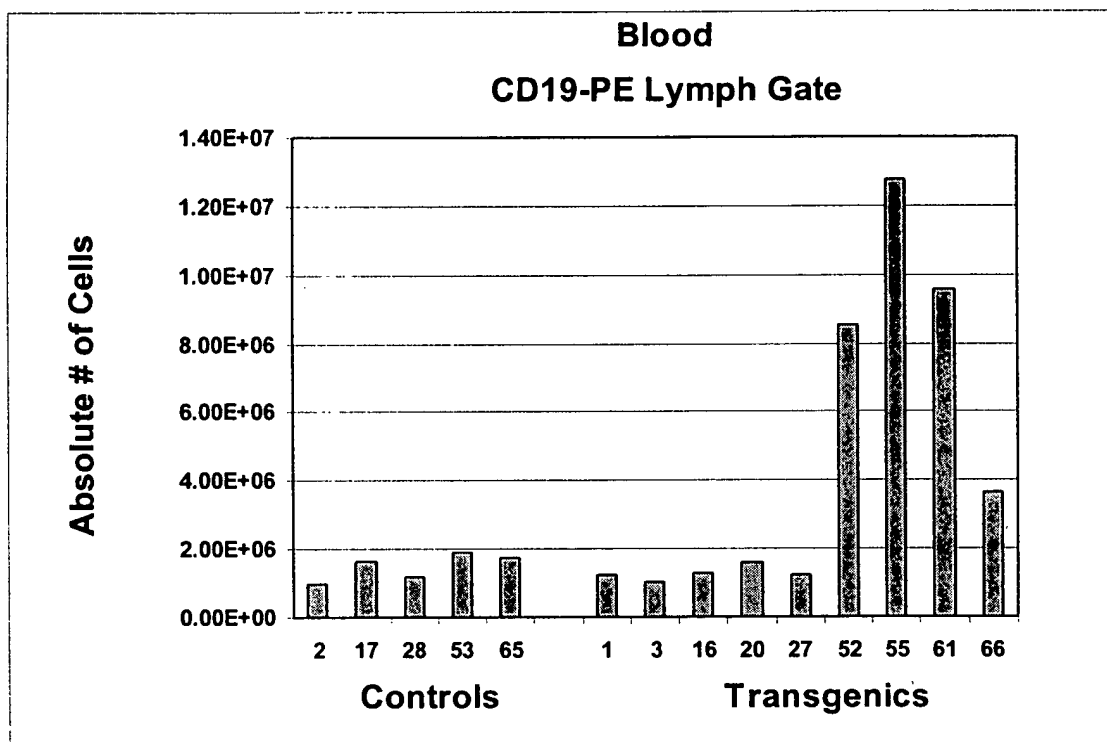


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Figure 11



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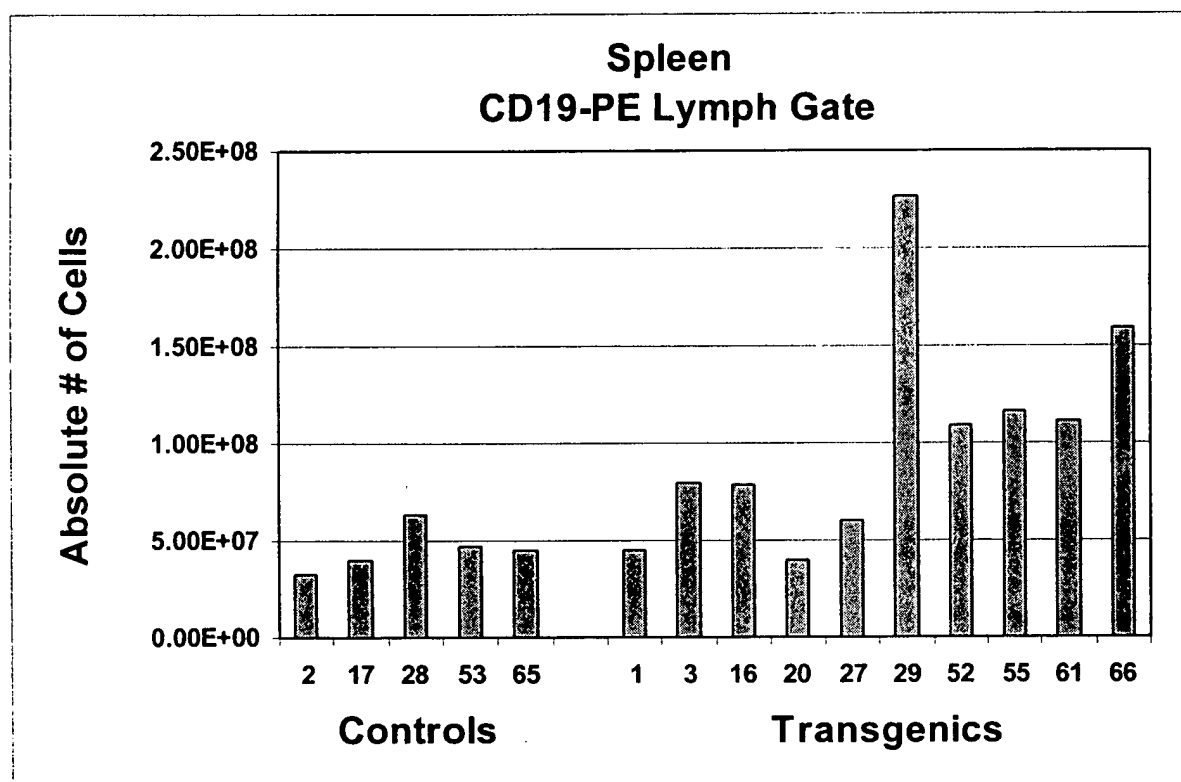
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Figure 12



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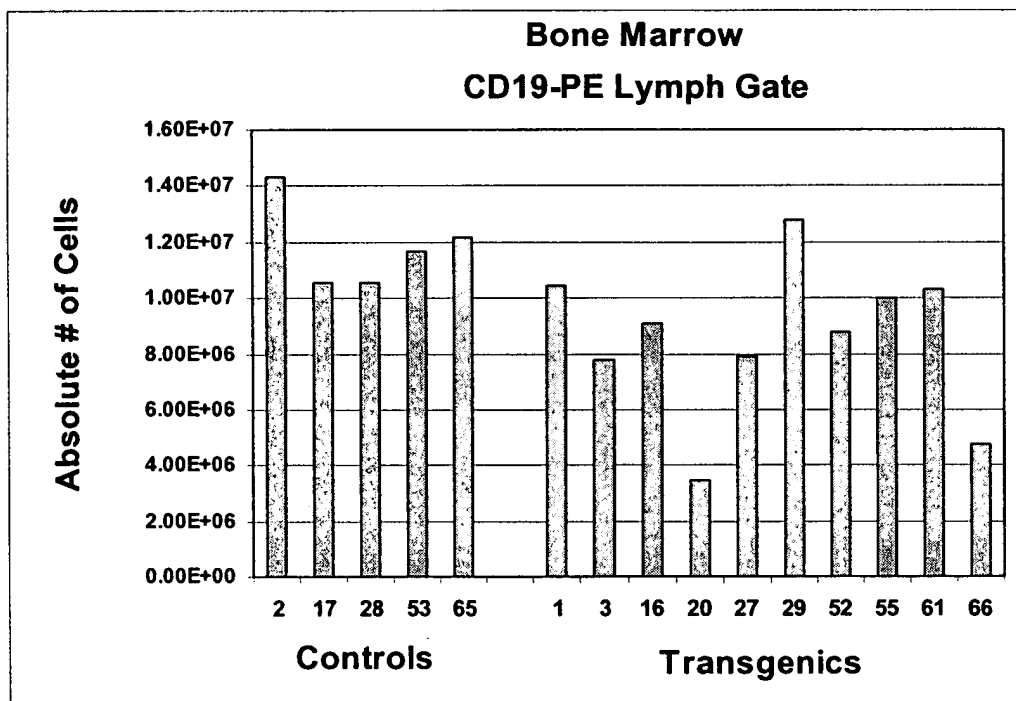
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Figure 13



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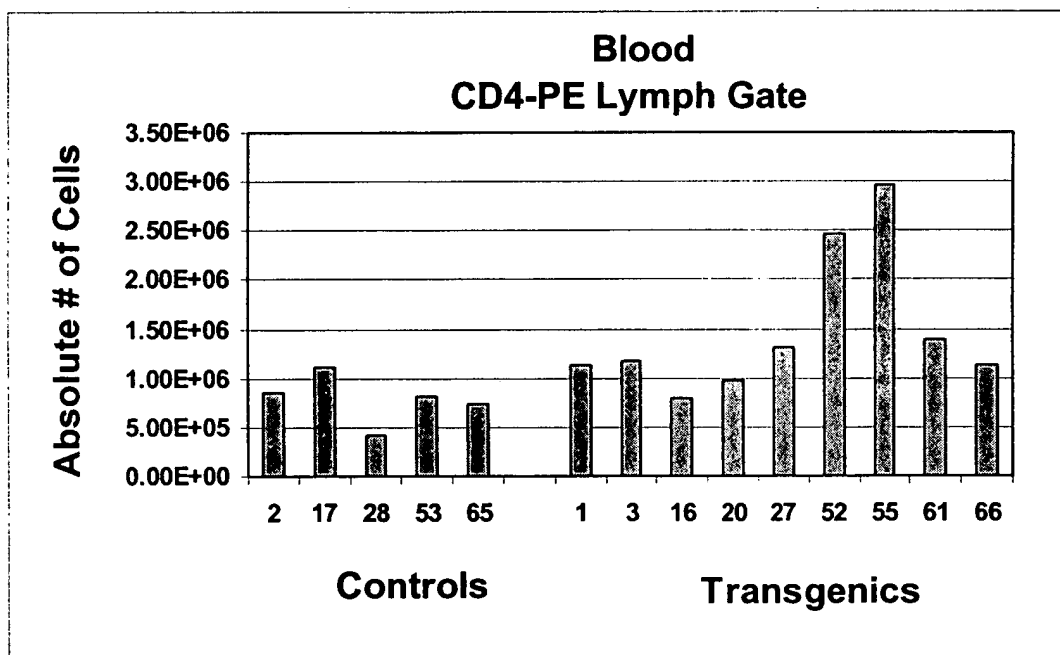
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Figure 14



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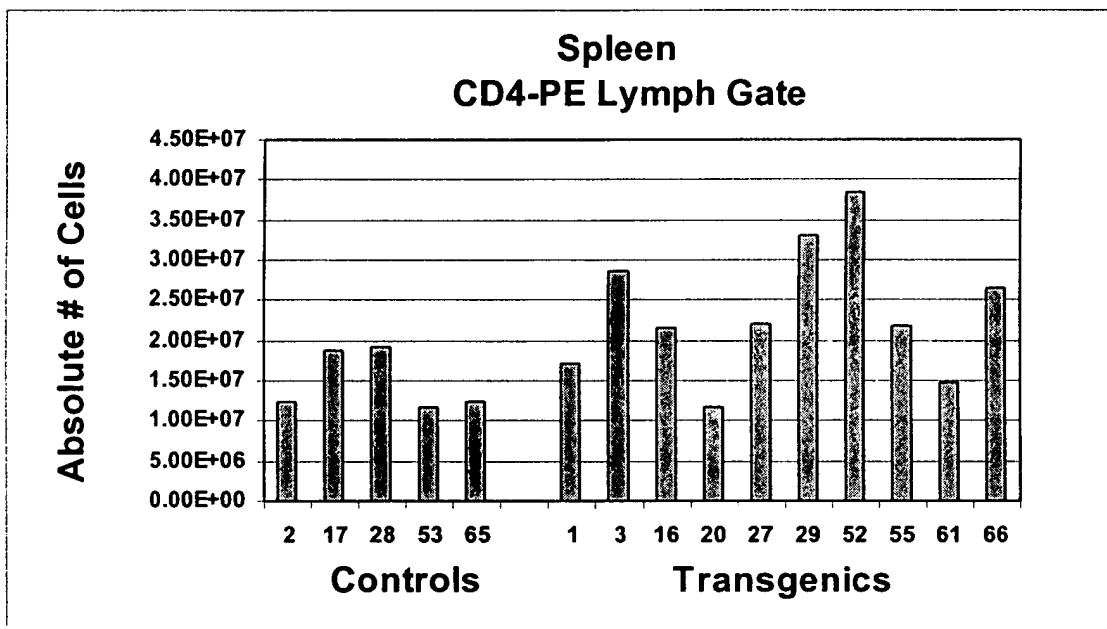
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Figure 15



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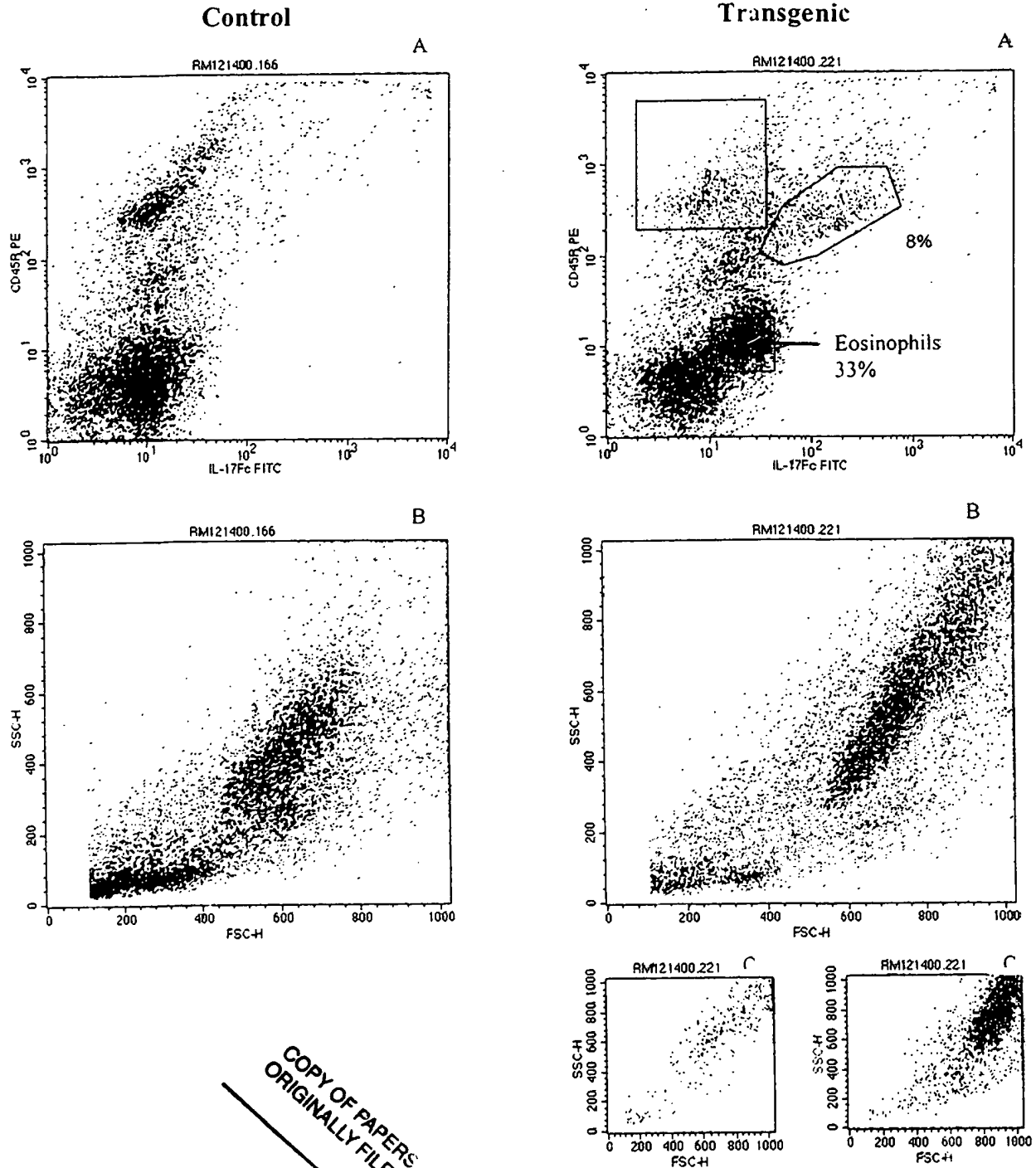
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Figure 16

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CD45R+ CELLS EXPRESSING IL17Br IN
TRANSGENIC BONE MARROWCOPY OF PAPERS
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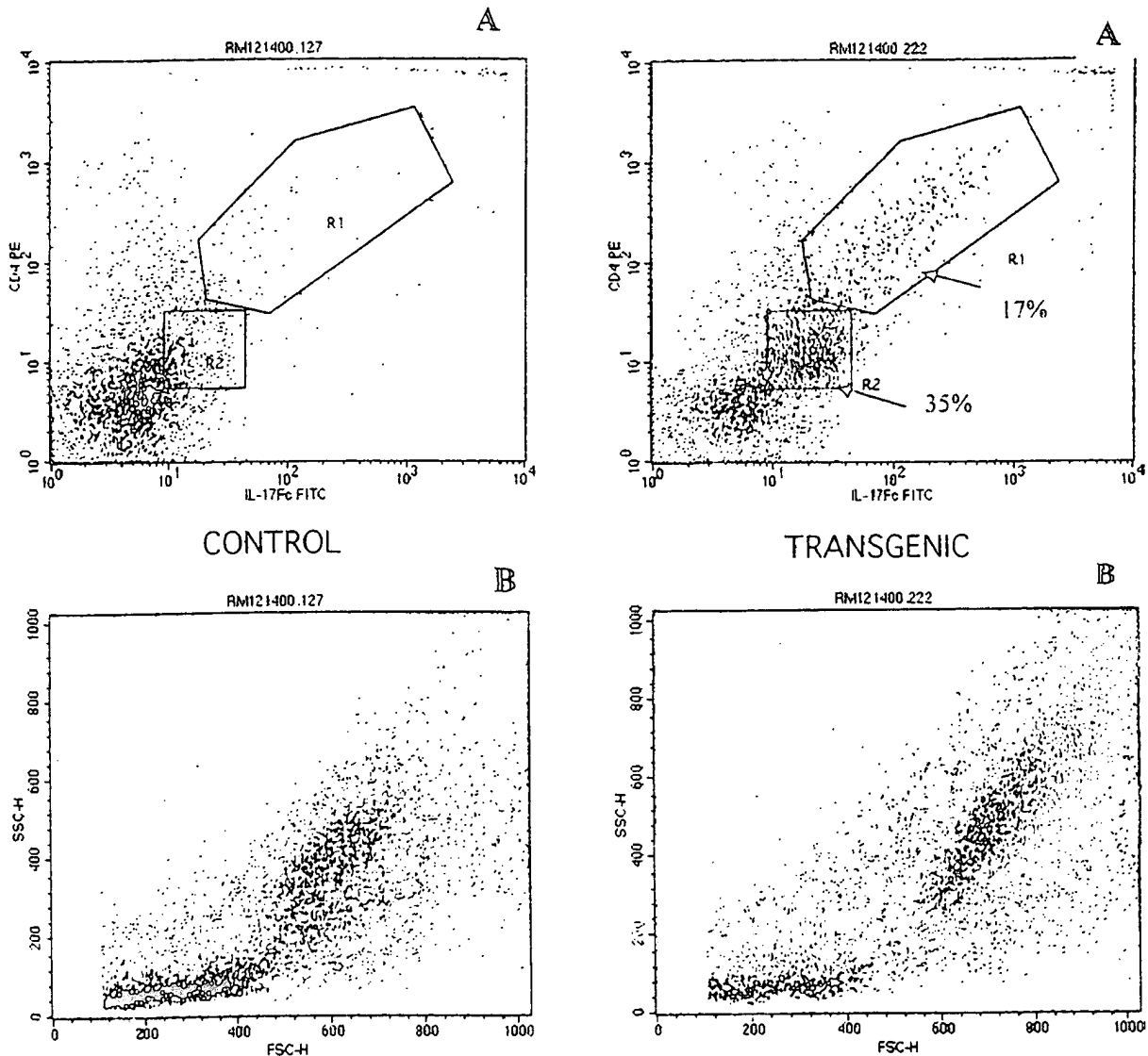
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Figure 17

CD4+ CELLS EXPRESSING
IL17Br IN TRANSGENIC BONE
MARROW



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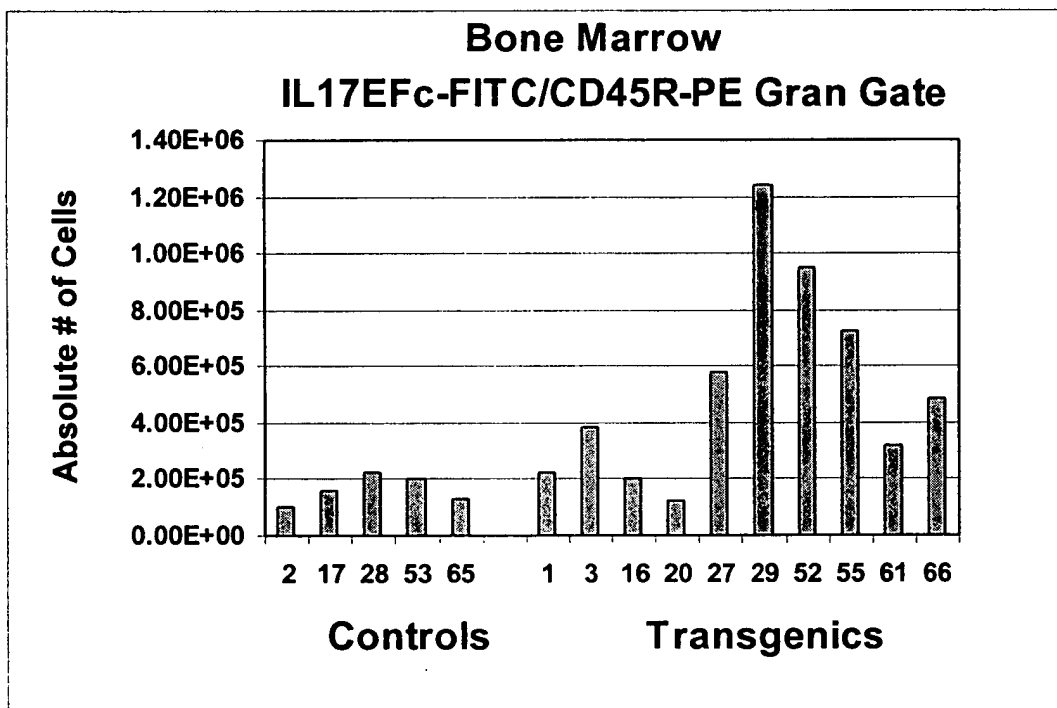
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Figure 18



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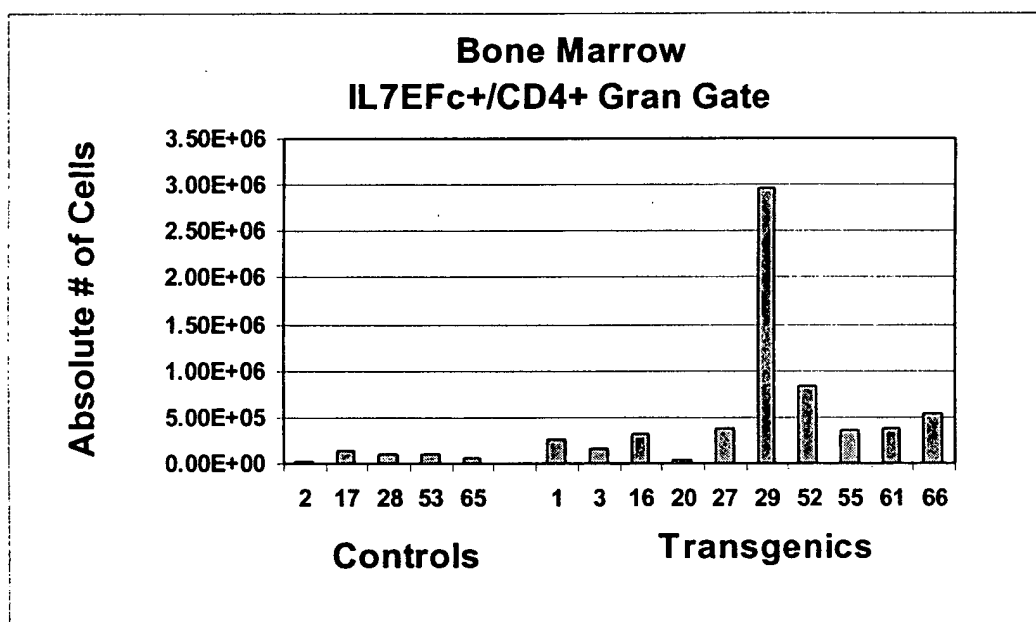
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Figure 19



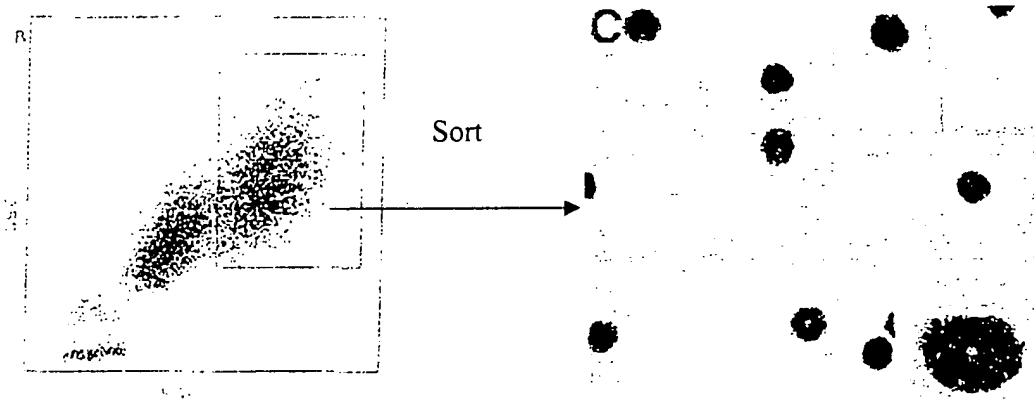
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Figure 20



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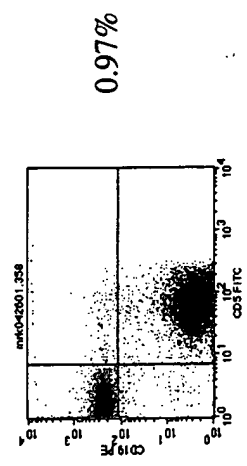
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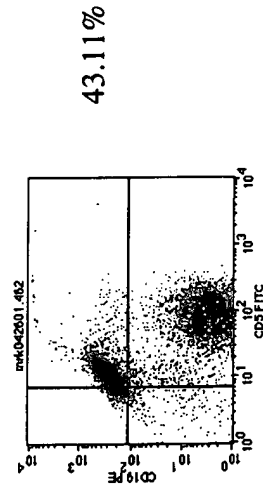
Figure 21A

Non-transgenic Control

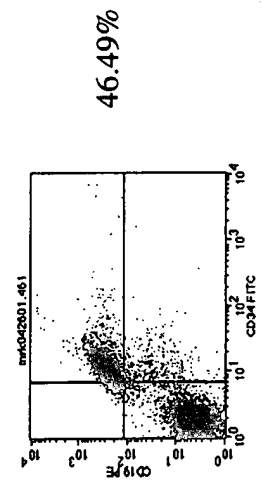
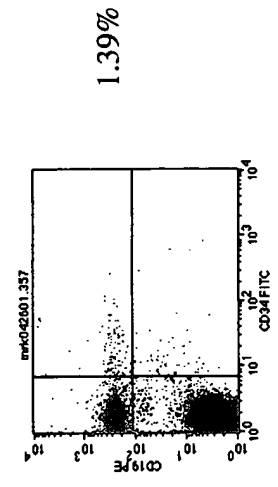
CD5+ on CD19+ Lymphocytes in Lymph Node



Transgenic



CD34+ on CD19+ Lymphocytes in Lymph Node



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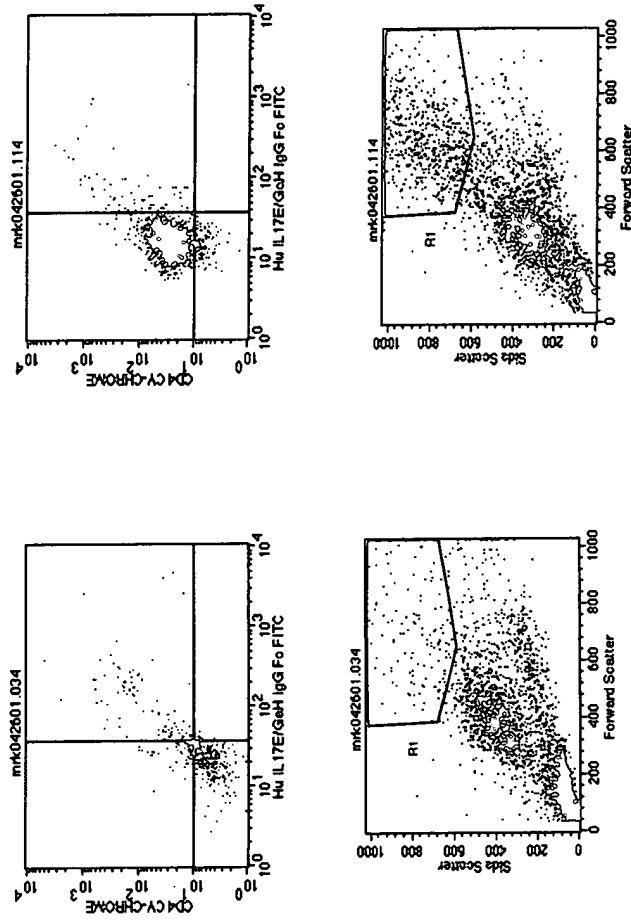
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Figure 21B
CD4 Expression on Eosinophils in Bone Marrow



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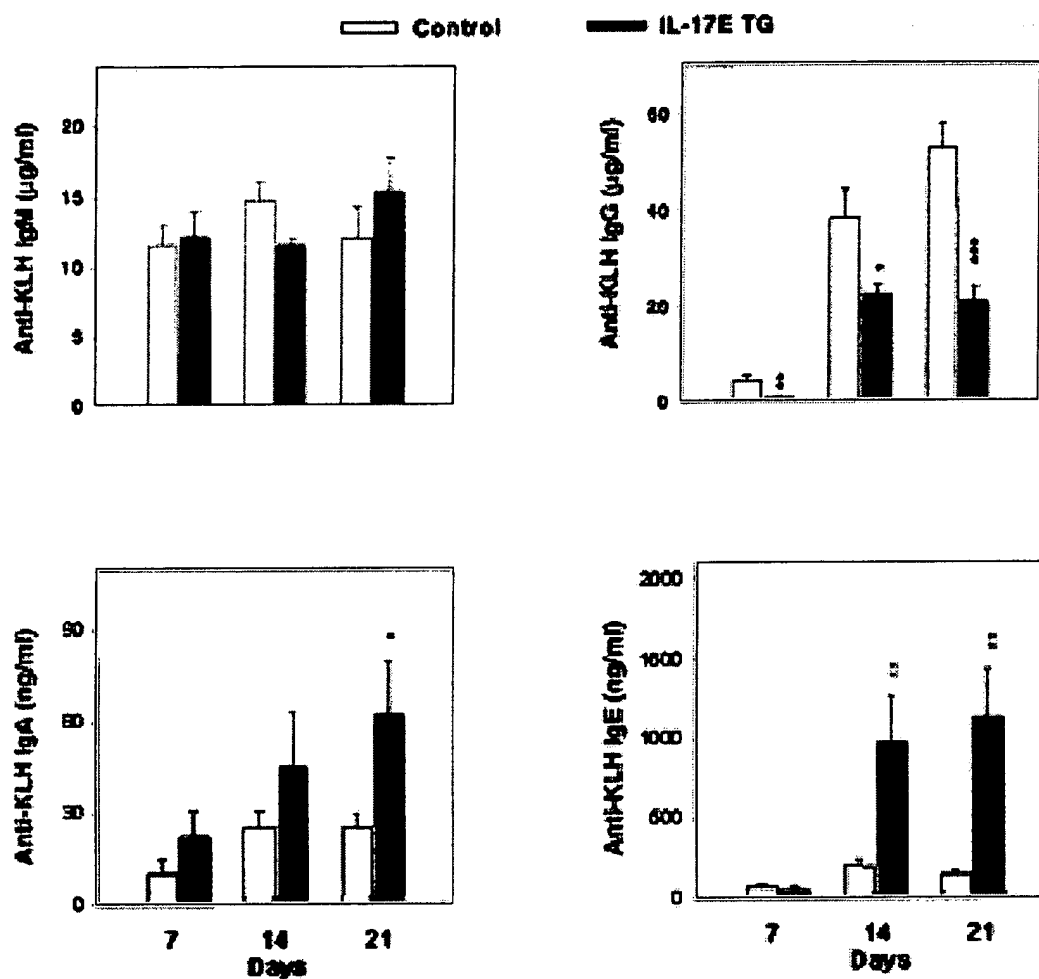


FIG.22

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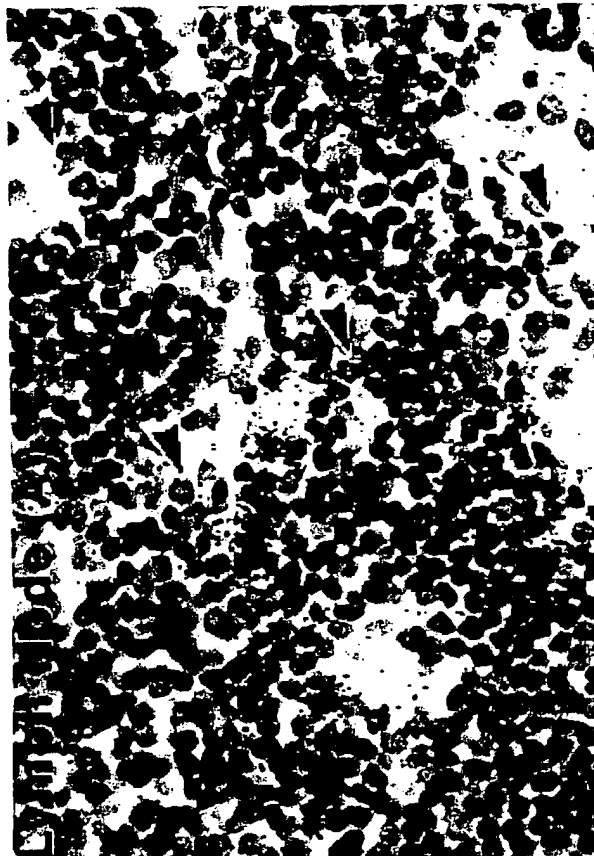


FIG.23

Lung (B)

Lung (A)

Mesentery (C)